REMARKS

Applicants have amended the claims in order to further clarify the definition of various aspects of the present invention. Specifically, Applicants have amended each of claims 18, 42 and 43 to recite that the complex administered to the animal, or added to the food or feed material, is a protein hydrolyzate/phospholipid complex; to recite that this complex contains at least 10 wt% of bound phospholipid, and to recite that the phospholipid is enzyme-modified phospholipid. Note, for example, pages 2 and 3 of Applicants' original disclosure; note also, for example, Test Groups 4, 8, 9 and 12-14, described, for example, on pages 9-15 of Applicants' specification.

Moreover, Applicants are adding new claims 49-54 to the application. Claims 49, 51 and 53, dependent respectively on claims 18, 42 and 43, recite that the complex contains 10-50 wt% of the bound phospholipid; and claims 50, 52 and 54, dependent respectively on claims 49, 51 and 53, recite that the complex contains 20-50 wt% of the bound phospholipid. Note, for example, the third full paragraph on page 3 of Applicants' specification.

Applicants respectfully submit that all of the claims presented for consideration on the merits by the Examiner patentably distinguish over the teachings of the references applied by the Examiner in rejecting claims in the Office Action mailed December 22, 2004, that is, the teachings of the publications by Sugano, et al., "Cholesterol-Lowering Activity Of Various Undigested Fractions Of Soybean Protein In Rats", in J. Nutr. (1990), pages 977-85; Sugano, et al., "The Hypocholesterolemic Action of the Undigested Fraction of Soybean Protein in Rats", in Atherosclerosis, 72 (1988), pages 115-122; Imaizumi, et al., "Influence of Saturated and Polyunsaturated Egg Yolk Phospholipids on Hyperlipidemia in Rats", Agric. Biol. Chem., 53 (9), 1989, pages 2469-74; Sirtori, et al., "Cholesterol-Lowering

and HDL-Raising Properties of Lecithinated Soy Proteins in Type II Hyperlipidemic Patients", in Ann. Nutr. Metab. 29 (1985), pages 348-357; and Williams, et al., "Intravenously Administered Lecithin Liposomes: A Synthetic Antiatherogenic Lipid Particle", in Perspectives in Biology and Medicine, 27 (3), 1984, pages 417-431, under the provisions of 35 USC 103.

It is respectfully submitted that these references as applied by the Examiner would have neither taught nor would have suggested such a method for improving the cholesterol metabolism of an animal, including administering a protein hydrolyzate/phospholipid complex containing at least 10 wt% of bound phospholipid, the bound phospholipid in the complex remaining bound to the protein hydrolyzate after being treated with a nonpolar organic solvent, and wherein the protein is soybean protein and the phospholipid is enzyme-modified phospholipid. See claim 18.

It is further respectfully submitted that these applied references would have neither disclosed nor would have suggested a method for lowering cholesterol or lipid level of an animal, or for producing food or feed, which includes administering, or adding to a food or feed material, the protein hydrolyzate/phospholipid complex as referred to previously in connection with claim 18, including the amount of bound phospholipid and wherein the phospholipid remains bound after treatment with a nonpolar organic solvent, and wherein the protein is soybean protein and the phospholipid is enzyme-modified phospholipid. Note claims 42 and 43.

Furthermore, it is respectfully submitted that the teachings of these applied references would have neither disclosed nor would have suggested the other aspects of the present invention as in the remaining, dependent claims being considered on the merits in the above-identified application, including (but not limited

to) wherein the enzyme-modified phospholipid is enzyme-modified lecithin obtainable by treating lecithin with phospholipase (see, e.g., claims 36, 45 and 48); and/or wherein the animal to which the complex is administered is human (see claims 38 and 46); and/or amount of bound phospholipid in the complex as in claims 49, 51 and 53, especially as in claims 50, 52 and 54.

The present invention is directed to decreasing cholesterol concentration in blood and in the liver.

In recent years, mortality from adult diseases, particularly cardiovascular disorders, is rapidly rising, and a correlation between occurrence of such disorders and cholesterol concentration in blood has been pointed out. Attempts have been made to lower the cholesterol concentration in blood by the use of specific food components, for example, various proteins such as soybean protein or soybean protein hydrolyzate; or, in other proposals, by the use of egg yolk phospholipid. See page 1, lines 15-30 of Applicants' application.

Attempts have also been made to lower cholesterol concentration in blood by use of a combination of lactalbumin, collagen, soybean protein, or wheat gluten, and soybean lecithin, or by the use of a textured soybean protein containing 6% of soybean lecithin. Note the paragraph bridging pages 1 and 2, and the first full paragraph on page 2, of Applicants' specification.

However, these prior techniques do not provide desired level of cholesterol reduction.

Against this background, Applicants provide a material providing unexpectedly better cholesterol reduction in the blood and in the liver. Applicants have found that by using a complex of a protein hydrolyzate/phospholipid, containing at least 10 wt% of bound phospholipid in the complex, the protein being soybean protein and the

phospholipid being an enzyme-modified phospholipid, unexpectedly better reduction of cholesterol is achieved. As to what is meant by the complex having bound phospholipid, attention is respectfully directed to the paragraph bridging pages 2 and 3 of Applicants' specification, wherein the term "bound phospholipid" is defined as a phospholipid which remains bound to a protein after being treated with a nonpolar organic solvent, such as petroleum ether.

It is respectfully submitted that protein hydrolyzate/enzyme-modified phospholipid complexes lower serum and liver cholesterol level more significantly than protein hydrolyzate containing phospholipid which is obtained by hydrolyzing soy protein (by pepsin) as in the Sugano references, discussed infra.

Specifically, it is respectfully submitted that the invention as presently claimed in the above-identified application, having the soy protein hydrolyzate/enzyme-modified phospholipid complex, provides unexpectedly better results, as compared with the applied prior art, as can be seen by the enclosed Declaration (unsigned). A signed copy will be submitted shortly. That is, unexpectedly superior cholesterol-lowering effect achieved by the presently claimed soybean protein hydrolyzate/enzyme-modified phospholipid complex, as compared to protein hydrolyzate containing phospholipid, can be seen in the enclosed Declaration, discussed in the following.

Composition of diets fed to male rats is shown in Table 1 on page 4 of the enclosed Declaration. Furthermore, the results in body weight gain, food intake, liver weight, serum and liver lipids for the rats tested, are shown in Table 2 on page 6 of the enclosed Declaration.

Attention is also directed to the Conclusion of this Declaration, set forth on pages 6 and 7 thereof. As set forth therein, content of serum total cholesterol of the

soy protein hydrolyzate/enzyme-modified phospholipid complex fed group was lower than that of the soy protein hydrolyzate fed group. Moreover, contents of serum LDL+VLDL cholesterol, liver total lipids, liver cholesterol, liver triacylglycerol and liver phospholipids of the soy protein hydrolyzate/enzyme-modified phospholipid complex fed group were significantly lower than those of the soy protein hydrolyzate fed group. In addition, content of serum HDL cholesterol and the ratio of HDL cholesterol to total cholesterol of the soy protein hydrolyzate/enzyme-modified phospholipid complex fed group were significantly higher than those of the soy protein hydrolyzate fed group.

It is respectfully submitted that this Declaration establishes unexpectedly better results for the present invention with respect to, e.g., the soy protein hydrolyzate containing phospholipid, supporting unobviousness of the presently claimed invention.

The Sugano article in J. Nutr. (hereinafter "first Sugano reference") discloses that undigested high-molecular-weight fraction (HMF) of soybean protein prepared after exhaustive digestion by microbial proteases significantly decreased serum cholesterol levels. This first Sugano reference described the results of a series of animal studies designed to examine the active component of the undigested fraction of soybean protein; and reports the results that the HMF obtained after peptic digestion is as effective as that obtained after microbial protease digestion in preventing the elevation of cholesterol in serum and liver by dietary cholesterol through interference with steroid absorption. Note the paragraph bridging the right-hand and left-hand columns on pages 983 and 984 of this article.

The article by Sugano, et al. in Atherosclerosis (hereinafter "second Sugano reference") discloses how soybean derived peptides which are resistant to bacterial

proteases and relatively abundant in hydrophobic amino acids exert a substantial hypocholesterolemic effect in rats compared to the parent protein. This second Sugano reference discloses that in feeding rats undigested high molecular fraction of the soybean protein, not only serum but also liver cholesterol levels were similar to those usually encountered in rats given diets free of cholesterol. Note the Summary on the first page of the second Sugano reference. Note also the Discussion beginning on page 120 of this reference, and in particular the first paragraph of this Discussion.

It is respectfully submitted that neither of the Sugano, et al. articles would have disclosed, or would have suggested, administering soybean protein together with the enzyme-modified phospholipid, much less the complex having at least 10 wt% of the enzyme-modified phospholipid, bound in the complex, as in the present claims. It is respectfully submitted that each of the Sugano, et al. articles is silent about soybean protein containing enzyme-modified phospholipid, much less soybean protein/enzyme-modified phospholipid complex, and is silent as to whether these materials can reduce serum or liver cholesterol levels.

It is respectfully submitted that the additional teachings of Imaizumi, et al. would not have rectified the deficiencies of either of the first or second Sugano references, such that the presently claimed invention as a whole would have been obvious to one of ordinary skill in the art.

Imaizumi, et al. reports on a study carried out to determine if dietary egg yolk phospholipid also exerts a hypocholesterolemic action in rats given a high cholesterol diet, and if this action is influenced by the constituent fatty acids. The egg yolk phospholipid suppressed the elevation of serum cholesterol irrespective of its fatty acid composition, while purified phosphatidylcholine had no effect,

suggesting that the ethanolamine portion is responsible for the hypocholesterolemic effect. This article goes on to state that the results found indicate that the hypolidemic effect of dietary egg yolk phospholipid can be modulated by the combination of the constituent fatty acids as well as the base moieties. See page 2469 of this article.

It is respectfully submitted that this article, either alone or in combination with either of the two Sugano references, would have neither disclosed nor would have suggested that a combination of soybean protein and enzyme-modified phospholipid together would have an effect on cholesterol, much less advantages achieved through use of the complex recited in the present claims, especially with the amount of bound, enzyme-modified phospholipid. For example, these references do not disclose, nor would have suggested, any effect of the soybean protein and enzyme-modified phospholipid on each other, e.g., as interfering with each of their effects separately on cholesterol.

Moreover, there is the following description at page 984, right-hand column, lines 16-21 of the first Sugano reference.

In addition, because the content of lipids originating from HMF is less than 3% in the diet, the surprising hypocholesterolemic effect of HMF cannot be attributed to the lipid component alone. Rather, it is plausible that the nitrogen components in HMF-E are responsible for its activity. [*Footnote omitted. Emphasis added.*]

Furthermore, it is respectfully submitted that these references clearly do not disclose, nor would have suggested, the complex as in the present claims, especially with amount of bound, enzyme-modified phospholipid, and advantages thereof as discussed in the foregoing.

Sirtori, et al. discloses a low-lipid diet with textured soy proteins containing 6% of lecithin (L-TVP). The article reports on the activity of this lecithinated product within a formal protocol in a multicenter study on type IIA patients, given both a complete and partial substitution of animal proteins in their diet. See the first paragraph in the left-hand column on page 349. This article goes on to disclose that in several studies, substitution of animal proteins with a textured vegetable protein product exerted a marked hypocholesterolemic activity in type II patients; and that in the study reported in the article, similar findings were obtained with a textured vegetable protein product containing 6% by weight of lecithin. Note the "Discussion" starting on page 353 of this article.

It is respectfully submitted that Sirtori, et al. does not disclose, nor would have suggested, use of soybean protein hydrolyzate, as in the present claims, or use of the enzyme-modified phospholipid, much less use of the complex including the recited amount of bound, enzyme-modified phospholipid, and advantages achieved thereby. Noting especially that Sirtori, et al. discloses textured soy proteins containing 6% of lecithin, it is respectfully submitted that this reference would have taught away from the present invention, including complexes containing the hydrolyzate and enzyme-modified phospholipid, in amounts as in the present claims.

It is respectfully submitted that the additional teachings of Williams, et al. would not have rectified the deficiencies of Sirtori, et al., such that the presently claimed invention as a whole would have been obvious to one of ordinary skill in the art. This article reports on a proposal that intravenously injected lecithin forms circulating liposomes, and would take up cholesterol from many sources, including the arterial wall; and that, in this way, lecithin liposomes become carriers of endogenous cholesterol, these liposomes being gradually removed from circulation

by the liver which catabolizes liposomes and excretes their cholesterol. Note the second paragraph on page 417; see also the paragraph bridging pages 419 and 420.

Even assuming, arguendo, that the teachings of Williams, et al. were properly combinable with the teachings of Sirtori, et al., such combined teachings would have neither disclosed nor would have suggested the presently claimed subject matter, including at least wherein a complex of protein hydrolyzate and enzyme-modified phospholipid was administered, the complex containing at least 10 wt% of bound, enzyme-modified phospholipid, and advantages thereof as discussed in the foregoing.

The contention by the Examiner on page 3 of the Office Action mailed December 22, 2004, that the criticality of the enzyme-modified phospholipid is not readily apparent to the Examiner, and, that the specification does not provide a definition or experiments conducted with this product, are respectfully traversed. Initially, it is respectfully suggested that criticality is only necessary where the Examiner has established prima facie case of obviousness. As seen in the foregoing, and as can be seen in a full review of the teachings of the applied prior art, it is respectfully submitted that the teachings of the applied references would have neither disclosed nor would have suggested use of enzyme-modified phospholipid, and, accordingly, it is respectfully submitted that the teachings of the references would have neither disclosed nor would have suggested (that is, would not have established a prima facie case of obviousness) a method utilizing complexes including the enzyme-modified phospholipid.

In addition, Applicants respectfully traverse the conclusion by the Examiner that the specification of the above-identified application does not include, inter alia

experiments conducted with this product. Note, for example, Test Groups 4, 8, 9 and 12-14 and the Test Examples in connection therewith, on pages 7-15 of Applicants' specification. See also, for example, Example 9 on page 19 of Applicants' specification. It is respectfully submitted that "enzyme-modified" would have been known by one of ordinary skill in the art, particularly in view of descriptions in connection therewith in Applicants' specification (note, for example, the last full paragraph on page 2 of Applicants' specification), such that one of ordinary skill in the art would have known what is meant by "enzyme-modified" phospholipid.

Furthermore, note the enclosed Declaration, showing unexpectedly better results achieved by the presently claimed invention using the complex including the enzyme-modified phospholipid, as discussed previously.

The contention by the Examiner on page 4 of the Office Action mailed December 22, 2004, that Applicants have not shown that the composition in the prior art is not in a bound form, is noted. The present claims specifically recite a characteristic of the phospholipid and the complex (that is, that the phospholipid remains bound to the protein hydrolyzate after being treated with a nonpolar organic solvent). The burden is on the Examiner, not Applicants, to show that the prior art has this feature. It is respectfully submitted that the Examiner has not satisfied this burden.

In view of the foregoing comments and amendments to the claims, reconsideration and allowance of all claims presently being considered on the merits in the above-identified application, are respectfully requested.

Docket No. 506.35379CC2
Serial No. 09/544,632
June 22, 2005

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Respectfully submitted,

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